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Comparative Genomics of *Vibrio cholerae* O1 Isolated from Cholera Patients in Bangladesh

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BACKGROUND

• Cholera remains an endemic disease in Bangladesh where this disease occurs in seasonal regularity with more than 100,000 cases annually (Ali et al; 2015). Recently, the severity of the disease has significantly increased in urban area since the emergence of the new variant of *Vibrio cholerae* O1 El Tor (Chowdhury et al; 2015).

•Molecular changes in *V. cholerae* have to be closely monitored as this information may help in understanding the changing genetic features of this pathogen in relation to the epidemiology of cholera.

•In this study, Whole Genome Sequencing (WGS) was utilized to investigate the current genomic profile of *V. cholerae* O1 strains, isolated from symptomatic patients in the low-income urban area of Arichpur, Dhaka, Bangladesh.

METHODS AND MATERIALS

During October 2015, three *V. cholerae* O1 strains (VC-1, 2 and 3) were isolated from rectal swabs of two patients living in households 588 m apart. One of the two patients was co-infected with two *V. cholerae* strains (VC-1 and VC-3). Major virulence factors, biotype and antimicrobial resistance genes were identified by WGS. A global phylogenetic tree was inferred using genome wide SNPs (Single Nucleotide Polymorphism) analysis

Sequencing Platform and Online Bioinformatics Tools

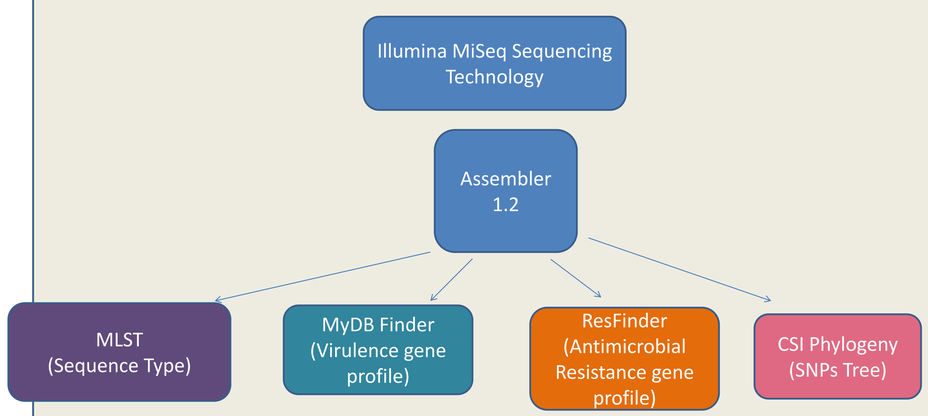

Table 1: Strain information

V. cholerae strain ID	Source	City/Country	Accession No.	Serogroup	Serotype	Biotype	Species-Serogroup			Biotype-specific		
							ompW	*rfbV-O1*	*wbfZ-O139*	*ctxB*	*rstR*	*tcpA*
VC_1	Rectal swab	Dhaka/Bangladesh	ERS1484954	O1	Inaba	El Tor variant	+	+	-	CC*	ET*	ET
VC_2	Rectal swab	Dhaka/Bangladesh	ERS1484955	O1	Inaba	El Tor variant	+	+	-	CC	ET	ET
VC_3	Rectal swab	Dhaka/Bangladesh	ERS1484956	O1	Inaba	El Tor variant	+	+	-	CC	ET	ET

Table 2: Virulence profile

VC strain ID	Virulence genes													Gene for 7th pandemic	*intSXT* gene (mobile genetic element)	Class I integron (*intI*)
	ctxA	*ctxB*	*tcpA*	*zot*	*ace*	*hlyA*	*stn*	*chxA*	*rtxA*	*toxR*	*ompU*	*mshA*	TTSS			
VC_1	+	+	+	+	+	+	-	-	+	+	+	+	-	+	+	-
VC_2	+	+	+	+	+	+	-	-	+	+	+	+	-	+	+	-
VC_3	+	+	+	+	-	+	-	-	+	+	+	+	-	+	+	-

Table 3: Resistance gene profile

Isolate ID	Antimicrobial Agent	Resistance genes
VC-1	Aminoglycoside	*strB*
	Phenicol	*catB9*
	Trimethoprim	*dfrA1*
VC-2	Aminoglycoside	*strA, strB*
	Phenicol	*catB9*
	Sulphonamide	*sul2*
	Trimethoprim	*dfrA1*
VC-3	Aminoglycoside	*strA, strB*
	Phenicol	*catB9*
	Sulphonamide	*sul2*
	Trimethoprim	*dfrA1*

RESULTS

• All three *V. cholerae* strains were El Tor variant of *Vibrio cholerae* O1 carrying standard classical ctxB genotype.

• The three strains are strictly clonal, 2 SNPs difference of VC-1 with VC-2 and 3, no SNP difference between VC-2 and 3. The rational behind the low number of SNPs in these Vc strains might be that the strains were isolated within a limited time frame (11 days apart) and from local outbreaks (two households are in the same community).

• The closest neighboring genomes in SNP based global phylogenetic tree were differed in 11 and 12 SNPs which were epidemic clones of *V. cholerae* O1 isolated in 2010 from Pakistan and Bangladesh respectively.

• All strains harbored multidrug resistance genes for aminoglycosides, phenicol, sulphonamide, and trimethoprim except VC-1 that lacked sulphonamide resistance genes. They lacked the integrase gene of the class I integron (*intI*) but harboured the SXT element (*int*SXT).

• The in silico MultiLocus Sequence Typing (MLST) revealed that these strains belonged to sequence type 69 which is similar to the pandemic strains (N16961 and MO45) and the Haitian epidemic strain (2010EL1786).

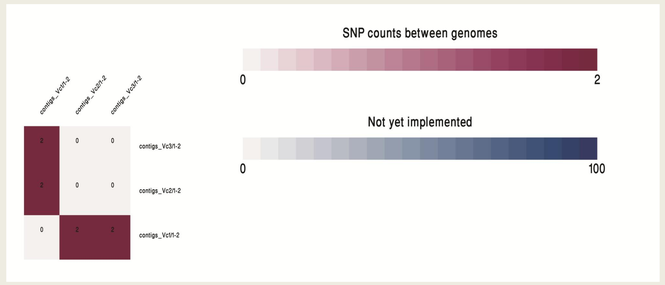

Figure 1: SNP matrix of the three study strains

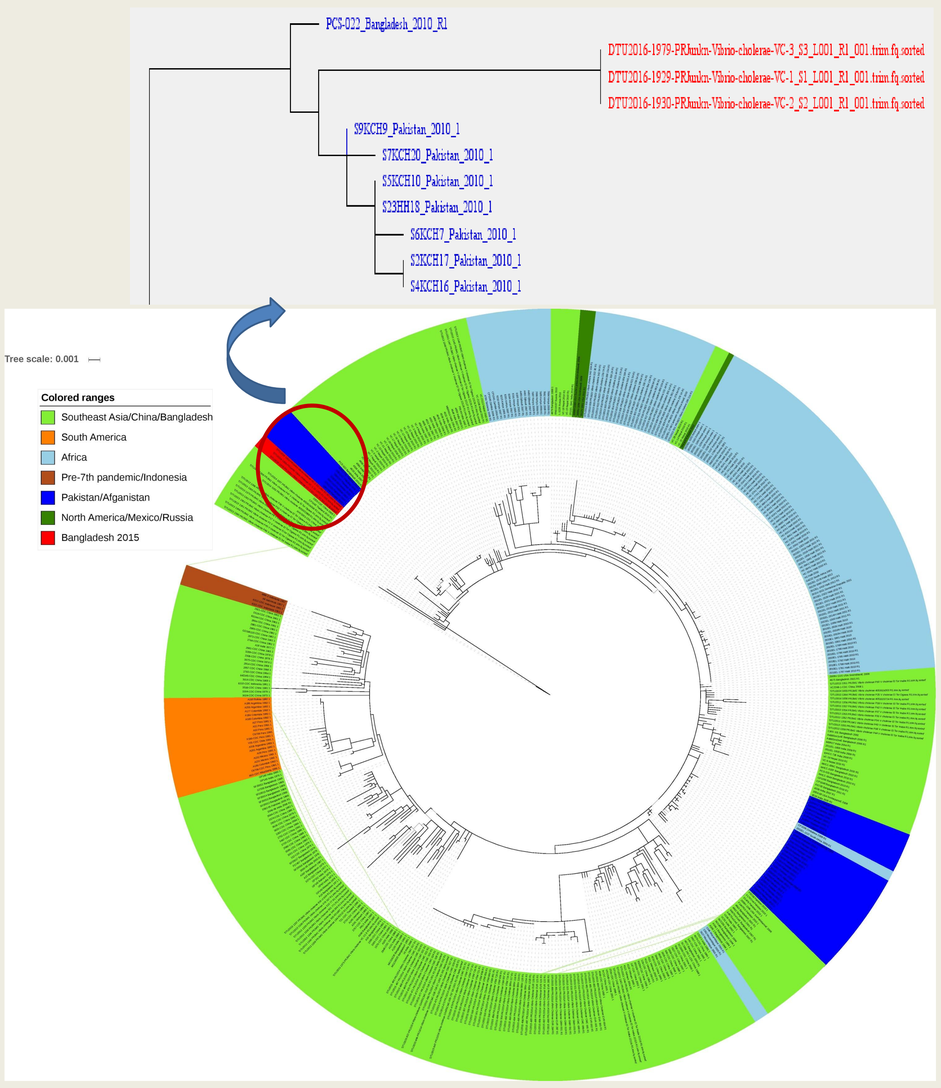

Figure 2: Global phylogenetic tree constructed with 352 database strains based on SNPs (Regions highlighted in colors)

CONCLUSIONS

• In this study, we used WGS and bioinformatics tools to analyze current genetic traits of clinical *V. cholerae* O1 circulating in urban household clusters of Bangladesh.

• The study contributed to understanding the epidemiology of *V. cholerae* in household patients in Bangladesh that ultimately can be applied for control measures and management of the emerging pandemic cholera in Bangladesh.

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